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THE REGIOSELECTIVE S → C AND S → N ALLYLIC REARRANGEMENT OF S-ALLYLTHIOIMIDATE

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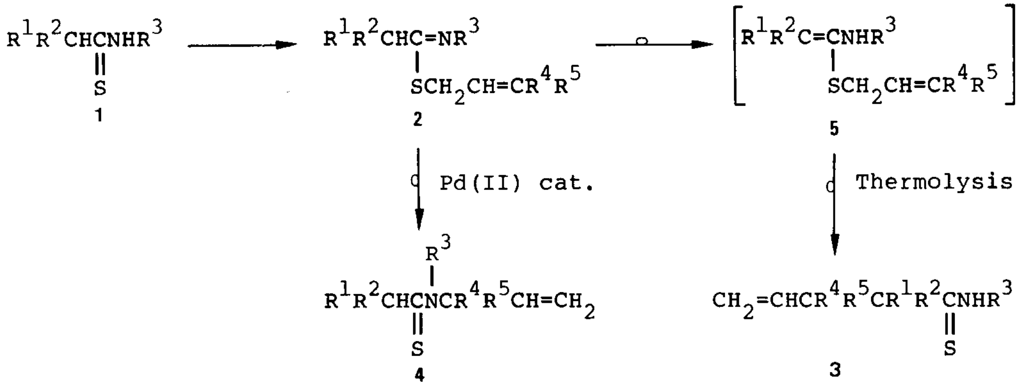
Summary. *The regioselective S → C and S → N allylic rearrangements of S-allylthioimidates are realized by thermolysis (160∿200°C) or palladium (II) catalysis (1∿10 mol% in refluxing THF), respectively.*

In these years the regio- and stereoselective C-C bond forming reactions have been deviced making use of the characteristic behavior of the thioamide group.[1] In addition to these, thioamide has been recognized as a versatile synthon by the development of the various high yield transformation methods to other functional groups (e.g., ketones,[2] amines,[3] enamines,[4] ketene S,N-[5] and S,S-acetals,[6] etc.). Compared with the tertiary thioamide, however, the chemistry of the secondary thioamide has been less disclosed.[7,8] Herein we report some interesting behavior of S-allylthioimidate (2) which is readily prepared by the allylation of thioamides: 2 undergoes selectively the S → C (the carbon α to the thiocarbonyl group) rearrangement to provide the C-allylated secondary thioamide or the S → N rearrangement to provide the N-allylated tertiary thioamide[9] by the selection of conditions.

S-Allyl-N-methylthiopropionylimidate (2b), upon heating as neat liquid at 160°C for 1 h under argon, provided the S → C allylic migration product, N-methyl-2-methylthio-4-butenoylamide (3b), in 95% yield (entry 2, Table I).[10]

Scheme I



Any other products, which might stem from the olefin isomerization to provide S-propenylthioimidate[11] or S → N allylic rearrangement[9, 12] to provide N-allyl-N-methylthiopropionamide, were not detectable. The present thermal S → C allylic migration seems to be general as judged by the results summarized in Table I, which covers various types of S-allylthioimidates. The complete inversion of allylic portion of S-crotyl to C-methallyl (entries 6 and 8, Table I) suggests that the S → C migration involves two sequential reactions, i.e., isomerization of 2 to ketene S,N-acetal (5) and the thio-Claisen rearrangement of 5 (Scheme I). Unfortunately no diastereoselectivity resulted and 3f was obtained as a diasteromeric mixture (1:1) (entry 6, Table I).[1f, 1g] As being general in these types of rearrangements,[13] the reactions forming the bonds between the tertiary and the secondary carbons required the higher temperatures and longer reaction times (entries 7 and 8, Table I). No reaction took place in the reaction between the tertiary carbons (entry 9, Table I).

Making marked contrast to these, in the presence of $PdCl_2$ (2 mol%, THF reflux for 16 h), 2e rearranged to provide a mixture of C- and N-allylated thioamides (3e and 4e, respectively) in a ratio of 81:19 (entry 2, Table II). Under the same conditions except for the absence of $PdCl_2$, 2e was recovered completely. These results clearly indicate that $PdCl_2$ catalyzes both the S → N rearrangement (probably caused by the coordination of $PdCl_2$ to the sulfur atom of 2)[9] and the isomerization of 2 to ketene S,N-acetal 5 (probably caused by the coordination of $PdCl_2$ to the nitrogen atom of 2). In order to achieve the selective S → N allylic rearrangement, we examined the reactions taking the HSAB principle[14] as a guide. This proved to work nicely and the striking improvement of the ratio of the S → N to the S → C rearrangements was observed by replacing $PdCl_2$ with the softer Lewis acid, $Pd(OAc)_2$ (entry 3, Table II). In a practical sense, the substitution of N-phenyl for N-CH_3, which might correspond to making the nitrogen atom the harder Lewis base, is profitable. The results of the palladium catalyzed S → N allylic rearrangement, together with those of the corresponding thermal S → C rearrangement, are summarized in Table II, which demonstrates the migration of 2 proceeds highly selectively either in a S → C or in a S → N fassion depending on the conditions.

The ease of the present reaction may be augmented in the following experiments, with which the selective S → C and S → N allylic rearrangements are performed: For the S → C rearrangement (entry 7, Table II), thioimidate (2*l*) is heated as neat liquid at 200°C for 1 h under argon (as a matter of convenience by using a Kugel rohr apparatus under slightly reduced pressures) The reaction mixture is directly subjected to a column purification (silica gel, benzene as an eluent) to provide N-phenyl-2-allyl-thiopentanoylamide (3*l*) in 76% yield; mp. 68.5 °C (from benzene-hexane). ^1H NMR (in CCl_4, TMS)

Table I. The S → C Rearrangement of S-Allylthioimidates 2 (R^3= CH_3)[1]

Entry	Thioimidate 2					Reaction Conditions[2]		Yield of 3[3]
		R^1	R^2	R^4	R^5	Temp (°C)	Time (h)	(%)
1	2a	H	H	H	H	170	1	3a (75)
2	2b	Me	H	H	H	160	1	3b (95)
3	2c	Et	H	H	H	170	1	3c (89)
4	2d	Ph	H	H	H	160	1	3d (95)
5	2e	Me	Me	H	H	160	1	3e (81)
6	2f	Me	H	Me	H	160	1	3f (82)[4]
7	2g	Me	H	Me	Me	200	4	3g (39)
8	2h	Me	Me	Me	H	200	8	3h (64)
9	2i	Me	Me	Me	Me	200	4	3i (0)[5]

Table II. The Selective S → N and S → C Rearrangement of S-Allylthioimidate
2 (R^4= R^5= H).[1]

Entry	Thioimidate 2				Reaction Conditions[2]	Yield[3]	Ratio
		R^1	R^2	R^3		(%)	(3/4)[6]
1	2e	Me	Me	Me	neat, 160°C, 1 h.	81	100/0
2	2e	"	"	"	$PdCl_2$(2 mol%), 65°C, 16 h.	87	81/19
3	2e	"	"	"	$Pd(OAc)_2$(10 mol%), 65°C, 24 h.	42	4/96
4	2j	Me	Me	Ph	$PdCl_2(PhCN)_2$(1 mol%), 65°C, 21 h.	87	2/98
5	2k	H	H	Ph	neat, 200°C, 1h.	73	100/0
6	2k	"	"	"	$PdCl_2(PhCN)_2$(1 mol%), 65°C, 24 h.	81	0/100
7	2l	n-Pr	H	Ph	neat, 200°C, 1 h.	76	100/0
8	2l	"	"	"	$PdCl_2(PhCN)_2$(1 mol%), 65°C, 6 h.	80	0/100
9	2m	Ph	H	Ph	neat, 200°C, 1 h.	93	100/0
10	2m	"	"	"	$PdCl_2(PhCN)_2$(1 mol%), 65°C, 24 h.	94[7]	15/85

1) For the structures of 2, 3, and 4, see Scheme I.

2) See the experimental part in the text.

3) Yield refers to the (combined) isolated yield of 3 (and/or 4). All new compounds showed satisfactory spectral and analytical data.

4) 3f is obtained as a diastereomeric mixture (1 : 1).

5) Starting material (2i) is recovered completely.

6) Ratio is determined by means of VPC and/or ^1H NMR.

7) Yield is based on the 71% conversion.

δ 0.9∿2.0 (m, 7 H), 2.1∿2.7 (m, 3 H), 4.9∿5.2 (m, 2 H), 5.5∿6.0 (m, 1 H), 7.0∿7.7 (m, 5 H), and 8.95 (br.s, 1 H). IR (KBr disk, in cm^{-1}) 3230(s), 1595(m), 1535(s), 1495(m), 1420(s), 1320(s), 915(m), 765(m), and 700(m). Mass (m/e, relative int.) 233(1), 191(29), 190(29), 170(47), and 77(100). For the S → N rearrangement (entry 8, Table II), a solution of 2l (1 mmol) and PdCl$_2$(PhCN)$_2$ (0.01 mmol) in dry THF (5 ml) is refluxed for 6 h under argon. After the evaporation of THF, the residue is directly subjected to a column purification (silica gel, benzene) to give N-phenyl-N-allyl-thiopentanoylamide (4l) in 80% yield; bp. 150°C/1.5 mmHg. ^{1}H NMR (CCl$_4$, TMS) δ 0.8∿1.9 (m, 7 H), 2.43 (t, J = 7 Hz, 2 H), 4.8∿5.3 (m, 4 H, containing δ 4.9, d, J = 7 Hz, 2 H), 5.7∿6.4 (m, 1 H), and 7.1∿7.6 (m, 5 H). IR (neat film, cm^{-1}) 1640(w), 1490(s), 1440(s), 1400(s), 1235(m), 1070(m), 960(w), 925(m), and 700(s). Mass (m/e, relative int.) 233 (10), 218(22), 160(100), and 104(54).

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